

**REMARKS/ARGUMENTS**

Claims 2-37 and 39-54 were under examination. In this amendment claims 19, 20, 37 and 50 are cancelled and claims 43 and 51 are amended. Claim 51, from which the remaining claims depend, has been amended to specify that the device comprises a flow control system responsive to the detection apparatus and adapted to direct biological material into a selected branch channel and to reverse the direction of movement of biological material that has been directed into a selected branch channel. A reversible flow control system finds support in the specification and, for example, in original claims 20, 37 and 50.

In the most recent Office Action, various combinations of claims were rejected as allegedly anticipated under 35 USC §102(a) over Blankenstein; 35 USC §102(e) over Ramsey; 35 USC §102(b) over Kamentsky; and/or 35 USC §102(e) over Gourley. As noted, the claims as now amended relate to a device having a flow control system adapted to reverse the direction of movement of the biological material in a branch channel. The Kamentsky reference and Gourley reference clearly do not describe a device with a reversible system as evidenced by the fact that neither reference was cited by the Examiner in a rejection of any one of previously pending dependent claims 20, 37 and 50, which related to reversible flow. Accordingly, these references do not anticipate the instant claims and will not be discussed further here (except to emphasize that Applicants do not necessarily acquiesce to the Examiner's characterization of these references or their relationship to the previously pending claims).

The Office did cite the Blankenstein and Ramsey references in a rejection of at least one of claims 20, 37 and 50. Applicants respectfully submit that the instant claims were not anticipated by either reference. In the remarks below, Applicants first describe the claimed invention, and then discuss Blankenstein and Ramsey in turn.

**The Reversible Flow Control of the Claimed Invention**

The reversible flow control disclosed in the instant specification permits a change in the direction of flow of the sorted material, and can be used to increase the accuracy and/or speed of sorting of biological material, for example by allowing for confirmation of a sorting decision,

selection of particular branch channel, or correction of an improperly selected channel. The specification describes one use of the reverse flow control of the present invention at page 29:

A "reversible" sorting algorithm can be used in place of a "forward" mode, for example in embodiments where switching speed may be limited. For example, a pressure-switched scheme can be used instead of electro-osmotic flow and does not require high voltages and may be more robust for longer runs. However, mechanical constraints may cause the fluid switching speed to become rate-limiting. In a pressure-switched scheme the flow is stopped when a cell of interest is detected. **By the time the flow stops, the cell may be past the junction or branch point and be part of the way down the waste channel. In this situation, a reversible embodiment can be used. The system can be run backwards at a slower (switchable) speed (e.g., from waste to inlet), and the cell is then switched to a different branch or collection channel. At that point, a potentially mis-sorted cell is "saved", and the device can again be run at high speed in the forward direction.** This "reversible" sorting method is not possible with standard FACS machines. FACS machines mostly sort aerosol droplets which cannot be reversed back to the chamber, in order to be redirected. The aerosol droplet sorter are virtually irreversible. Reversible sorting is particularly useful for identifying rare cells (e.g., in molecular evolution and cancer cytological identification), or cells few in number, which may be misdirected due to a margin of error inherent to any fluidic device. The reversible nature of the device of the invention permits a reduction in this possible error."

Thus, Applicants teach reversing the direction of flow in of biological material in a branch channel.

#### Blankenstein

The Office states that Blankenstein disclosed reversible flow, citing page 24, line 36 to page 25, line 4 of WO 98/0267 (see Office Action the top of page 9). Blankenstein described a device for sorting particles. The section of Blankenstein cited by the Office refers to Figure 8, which is reproduced below for convenience. In the device of Figure 8 flow speed is controlled using syringe pumps that "suck the sample and buffer . . . through [a] separation flow channel." Blankenstein page 24, lines 28-29. Blankenstein explains that when one or both of the syringe pumps need to be emptied the motors driving the syringe pumps 41, 42 are operated in the reverse direction of normal operation direction to empty the syringe pumps through 3-way valves 43, 44 into a waste container, not shown (Blankenstein sentence spanning pages 24 and 25).

Clearly, Blankenstein did not describe or suggest a device having a flow control system responsive to a detection apparatus, and adapted to direct biological material into a selected branch channel and to reverse the direction of movement of biological material that has been directed into a selected branch channel. Thus, Applicants request that this rejection be withdrawn.

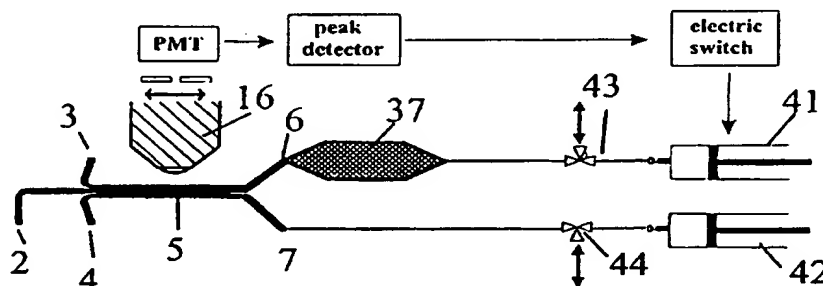
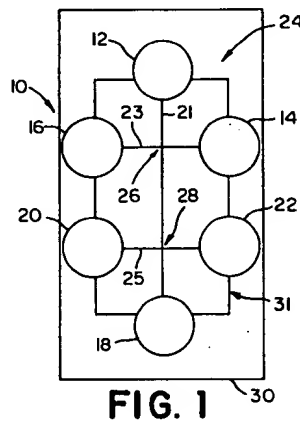


Fig. 8

Ramsey

The Office states that Ramsey disclosed reversible flow (citing col. 5, lines 2-5) and thus anticipated previously pending claim 20 (see Office Action the top of page 9). Ramsey described a microchip channel in which an electric field is used to spatially focus material traversing the material transport channel (see Abstract). Referring to Figure 1 of Ramsey (shown below for convenience) sample is transported from sample reservoir 12 to waste reservoir 18, passing through focusing chamber 28. Focusing chamber 28 is the region where two channels intersect, i.e., the channel extending between sample reservoir 12 and waste reservoir 18 intersects with the channel extending between focusing reservoirs 20 and 22. The electrical potentials at the focusing reservoirs 20 and 22 are controlled to laterally focus the sample transported from sample reservoir 12 to waste reservoir 18. By varying the relative potentials at the reservoirs, the degree of focusing can be adjusted. For example, for cathodic electroosmotic flow, the waste reservoir 18 is at a lower potential than all other reservoirs (col. 4, lines 24-27),

and as the potential at the sample reservoir is decreased, the sample field strength decreases, and the focusing field strength increases, resulting in a tighter focus of the sample stream (col. 4, lines 62-66). Figure 4, which is discussed at col. 5, lines 2-5 of Ramsey shows the focusing effect of varying the potentials at the reservoirs. At col. 5, lines 1-5, Ramsey notes that if the potential at the channel intersection defining the focusing chamber is adjusted so that it exceeds the potential applied to the sample reservoir the direction of transport in the sample channel reverses. It is this section that is asserted by the Office to disclose reversible flow. However, the cited section is merely an illustration by Ramsey of the effect of varying electrical potential in device reservoirs. Ramsey does not suggest the potential should be changed to reverse the direction of flow. In fact, reversing flow would appear to interfere with the functioning of the device. Clearly, nothing in Ramsey described or suggested a device with a flow control system *responsive to a detection apparatus and adapted to reverse the direction of movement of a biological material*, as instantly claimed. Thus, Applicants request that this rejection be withdrawn.



Rejections Under 35 USC 103(a)

Applicants believe all rejections under 35 USC 103(a) set forth by the Office are moot in view of the amendments to the claims specifying a reversible flow control system. None of the references individually or in combination suggested a device with a flow control system responsive to a detection apparatus and adapted to reverse the direction of movement of a biological material, as instantly claimed. For this reason, Applicants request that these rejections

be withdrawn.

Claim Objections

Claim 19 was objected to as duplicative and has been cancelled.

Obviousness-Type Double Patenting

Applicants believe the rejections for obviousness type double patenting articulated in paragraphs 18-21 and 23-26 of the Office Action are moot in view of the amendments to the claims specifying a reversible flow control system. However, Applicants will address the double-patenting rejections asserted against claims 20, 37 and 50, because, as discussed above, these claims related to reversible flow.

In paragraph 22 of the Office Action, claims 20 and 37 were rejected as unpatentable over claim 1 of US 6,221,654 in view of Kamentsky and Blankenstein. However, claim 1 of the '654 patent does not recite reversible flow, and neither Kamentsky and Blankenstein suggested a flow control system responsive to a detection apparatus and adapted to reverse the direction of movement of a biological material, as instantly claimed, for the reasons discussed above. Accordingly, Applicants request this rejection be withdrawn.


In paragraph 27 of the Office Action, claim 50 was rejected as unpatentable over claim 1 of US 6,334,325 in view of Kamentsky and Blankenstein. However, claim 1 of the '325 patent does not recite reversible flow, and neither Kamentsky and Blankenstein suggested a flow control system responsive to a detection apparatus and adapted to reverse the direction of movement of a biological material, as instantly claimed, for the reasons discussed above. Accordingly, Applicants request this rejection be withdrawn.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

  
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